

These resources are intended to help you provide consistent and clear information about the issue of compliance to hormonal therapy in the treatment of breast cancer. Many of these key points may also prove valuable in communicating the importance of compliance to all oral therapies in the treatment of other cancers.

Key Points to Share

- 1. Oral drug therapies are increasingly common in the treatment of many cancers, especially breast cancer, and for that reason, the medical community needs to understand that compliance to a drug regimen is essential to that treatment's success. However, research indicates that compliance is a very common problem.**
Supporting facts:
 - A recent Harris poll revealed that one in three (33%) U.S. adults who have been prescribed drugs to take on a regular basis report that they are often or very often non-compliant with their treatment regimes.¹
 - Data presented at the Compliance Strategic Initiative (CSI) symposium indicated that non-compliance rates for many chronic drug therapies may be as high as 40 percent over a five-year course of treatment.²
 - One study on hormonal therapies for breast cancer found that after four years of therapy, compliance rates among women decreased to 50 percent.² When this rate is applied to the approximately 500,000 breast cancer patients eligible for such therapy, as many as half of them may not be reaping the full benefits of their drug regimens.
 - Further, a study of tamoxifen discontinuance in women 55 years and older demonstrated that 15 percent of study participants had stopped taking their oral therapy during a nearly three-year follow up period.³
- 2. Studies have shown that hormone receptor-positive postmenopausal women with breast cancer greatly reduce their risk of recurrence by taking their hormonal therapy as prescribed by their physician. Supporting facts:**
 - When a woman with breast cancer is a candidate for post-treatment oral hormonal therapy following chemotherapy and/or radiation, studies have shown that she may reduce her chance of recurrence 12 percent by taking the drug one year, 29 percent by taking the drug for two years, and 47 percent by taking the drug up to five years.⁴
 - Poor adherence to medication regimens in general is common and contributes to substantial worsening of disease, death and increased healthcare costs.⁵
- 3. Not enough information is available about compliance. Education and an open physician-patient dialogue are critical to ensure that patients understand the benefits and risks of their medication, that breast cancer can recur and the chances of recurrence are higher in some women, and that they have the support they need to help them with their medication and side effects. Supporting facts:**
 - A review of approximately 50 healthcare Web sites, led by CSI co-sponsor CancerCare, shows that less than half mention compliance or adherence. Of

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those that do, only one in three ever mention it in the context of cancer treatment.

- One study that analyzed oncologists' discussions about adjuvant hormonal therapy with post-menopausal patients revealed that⁶:
 - Oncologists and patients exhibit good rapport and have open communication but the current dialogue is not sufficient to drive compliance
 - Hormonal therapy discussions differ from those on chemotherapy. Conversation displays a lack of urgency and emotion unlike a chemotherapy discussion where emotion is high. Patients are seen as, in some way, "cured" and that they are "given their lives back".
- Patient, physician and healthcare system barriers all contribute to non-compliance as a "major public health problem."⁷

4. **The CSI is committed to developing resources and strategies that will support women to help them stay compliant, thus reducing their risk of a breast cancer recurrence.**

Frequently Asked Questions

<i>ABOUT THE COMPLIANCE STRATEGIC INITIATIVE</i>

Q. What is the Compliance Strategic Initiative (CSI)?

A. The Compliance Strategic Initiative is an initiative comprised of national patient advocacy and support organizations, professional healthcare associations, and oncology professionals that are committed to addressing the issue of hormone therapy compliance in individuals with breast cancer.

The goals of the CSI are to:

- raise awareness about the importance of taking hormonal breast cancer therapies as prescribed to reduce the risk of breast cancer recurrence
- better understand therapy non-compliance
- provide education and resources to address the non-compliance issue and improve survivorship

Q. Why was the CSI initiative formed?

A. As the past U.S. Surgeon General, C. Everett Koop, M.D., stated, "Drugs don't work in patients who don't take them."

Studies indicate that five years of adjuvant hormonal therapy in individuals with breast cancer prolongs survival and reduces the risk of recurrence. Oral medications are playing an increasingly important role in the treatment and management of cancer,

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particularly in the treatment of breast cancer. And yet, little is known about how well cancer patients adhere to these regimens.

A recent Harris Poll on *general* prescription compliance indicates that typically one-third of all patients do not adhere to taking their medications as prescribed.¹

The CSI was formed to:

- raise awareness about the importance of taking hormonal breast cancer therapies, as prescribed
- better understand the issues surrounding therapy non-compliance
- identify and recommend educational resources for patients and healthcare providers to help address non-compliance and improve survivorship.

Q. Who is involved with this initiative?

A. Four organizations formed the steering committee to lead the CSI. They are:

- **American Cancer Society** – a nationwide, community-based, voluntary health organization dedicated to eliminating cancer as a major health problem by preventing cancer, saving lives, and diminishing suffering from cancer through research, education, advocacy, and service.
- **CancerCare** – a national, non-profit organization providing free professional support services to anyone affected by cancer, including people with cancer, caregivers, children, loved ones, and the bereaved.
- **National Surgical Adjuvant Breast and Bowel Project (NSABP)** – a clinical trials cooperative group supported by the National Cancer Institute (NCI).
- **Y-ME National Breast Cancer Organization** – founded in 1978 by two breast cancer survivors, Y-ME National Breast Cancer Organization’s mission is to ensure, through information, empowerment, and peer support, that no one faces breast cancer alone. The organization has affiliates throughout the U.S. that echo the mission and values of Y-ME in their role as breast health and breast cancer resources in their communities.

Support for this public health forum was provided through a charitable contribution from AstraZeneca.

At the CSI 2005 symposium, 47 participants representing 34 professional, academic, clinical and advocate organizations attended to provide insights, ideas and recommendations about breast cancer treatment compliance. The initiative is unique in its multi-disciplinary problem-solving approach to this important issue.

<i>ABOUT COMPLIANCE</i>

Q. What does compliance mean?

A. The extent to which a patient acts in accordance with the prescribed interval and dosing regime measured by percentage (taking as prescribed).⁸

Q. Why is compliance so important for women with breast cancer?

A.

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- According to the National Cancer Institute, in the U.S., one out of seven women will develop breast cancer in her lifetime.⁹
- In 2006, it is estimated that 212,920 new cases of invasive breast cancer are expected to occur among women in the U.S.¹⁰ More than 2 million women in the U.S. are living with a diagnosis of breast cancer.
- About 500,000 of these women are candidates for hormonal therapy and as a result of non-compliance, as many as one-half of them may not be reaping full benefits of available therapy.

For postmenopausal women whose breast cancer is hormone receptor-positive, studies have shown that additional or adjuvant treatment with a hormonal therapy can significantly reduce the risk of recurrence, particularly if the women stay on drug for the recommended five-year course of treatment. In one study of tamoxifen and compliance, overall compliance to the drug decreased to 50 percent by year four of the therapy.²

When a woman with breast cancer is a candidate for post-treatment oral medication, following chemotherapy and/or radiation, studies have shown she may reduce her chance of recurrence 12 percent by staying on drug one year, 29 percent by staying on drug for two years, and 47 percent by staying on drug up to five years.⁴

Q. Is there a compliance problem in the breast cancer community?

A.

Medication non-compliance is not unique to breast cancer. However, some of the factors that influence compliance and the impact of non-compliance are unique to this patient population. As uncovered at the CSI symposium, breast cancer patients feel that there are probably as many reasons for stopping treatment as there are women who stop.

Data presented at the CSI symposium indicated that hormonal therapy non-compliance rates among breast cancer patients decreased to 50 percent after four years of therapy.²

But the most significant issue facing breast cancer patients is the fact that, if untreated, the risk of recurrence is real:

- Medical literature documents that 50 percent of untreated patients will have a recurrence within 15 years post-diagnosis.
- Twenty-percent of node-negative patients will have a recurrence at five years.
- Forty-two percent of node-positive patients will have a recurrence at five years.⁴

Compliance with hormonal therapies does not prevent a recurrence, but significantly reduces the risk of a recurrence.⁴

Q. Why might a woman stop taking her medication?

A. As the CSI found, non-compliance among breast cancer patients has not been studied to a great extent. However, the following factors are often associated with adherence with oral medications:¹¹

- Significant behavioral change required
- Inconvenient or inefficient clinics

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- Inadequate supervision
- Complex treatment regimen
- Poor communication with healthcare providers
- Patient dissatisfaction with care
- Patient health beliefs weighing in favor of non-adherence
- Inadequate social support
- History of non-adherence
- History of mental illness

The CSI explored these issues and areas and reached several conclusions:

- Professional and public awareness about hormonal therapy compliance issues is low
- A communication gap exists between patients and providers, especially between those patients who don't feel empowered to voice concerns and physicians who may not typically have the time or skill set to listen well.
- And most important, that education and physician-patient dialogue are key to providing patients with the information and support they need to continue treatment.

Q. How many women with breast cancer might the compliance issue impact?

A. According to the American Cancer Society, approximately 212,000 women in the U.S. are diagnosed annually with breast cancer. Clinical data from the University of California San Francisco Medical Center indicate that approximately 60 percent of these survivors may be in the category of postmenopausal women with a hormone receptor-positive form of breast cancer. It is this category of patient – roughly 100,000 new women each year or a combined group of 500,000 women who are on a prescribed 5-year course of treatment – that is most affected by compliance to oral therapy.

Q: The compliance issue is surprising given how much awareness and educational support is available for breast cancer patients. Is this problem unique to the breast cancer community?

A. Compliance is an ongoing issue in a variety of patient populations. We feel this patient population merits a concerted effort in view of the effective medication to reduce their risk of a breast cancer recurrence. Studies have shown that women may reduce their chance of recurrence 12 percent by staying on drug one year, 29 percent by staying on drug for two years, and 47 percent by staying on drug up to five years.⁴

Q. I've heard that some women stop taking their medications because of side effects. Is this true?

A. There are many reasons a woman might stop taking her medication. It's not unusual for individuals who take any medication to experience side effects. It's important for women to discuss with their physicians ways to manage side effects. We encourage each woman to discuss side effects with her healthcare providers and to work with these providers to establish treatment options that work best for her. Many issues come into play – lifestyle, other medical conditions that the patient may have – so it is critical that patients and physicians have an open and honest dialogue to address and manage any side effect issues so that women can continue the medication.

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Q. Does insurance coverage or lack thereof play a factor in compliance?

A. In a study of compliance and the drug tamoxifen, the patient population analyzed was insured, and still, 50 percent of the women did not adhere to the drug as prescribed.²

Q. How does the CSI expect to combat the compliance problem?

A. By exploring the scope and causes of the issue, and by bringing together and encouraging discussion among multi-disciplinary healthcare experts who have different touchpoints to the woman during her decision-making process, the CSI has identified action items for further development. In addition, results of the 2005 CSI Symposium are being submitted for peer-review publication this year. Additional avenues for disseminating this important information are currently being explored.

Q. What are the action items that the CSI has identified to be further developed?

A. The CSI concluded that professional and public awareness about hormonal therapy compliance issues is low, and that a communication gap exists between patients and providers. That gap may be especially pronounced between those patients who do not feel empowered to voice concerns and the physicians who treat them. The tactical recommendations recommended for further development include:

- Development of CMEs and skill training to support compliance
- Greater involvement from nurses and social workers who may have opportunities to focus on communication and education
- Public awareness to address what to expect during hormonal therapy and to focus attention on the benefits of the treatment
- Development and implementation of a “patient navigation” model that supports the patient throughout the course of care, especially after the acute phase of disease and treatment, when patients are apt to feel forgotten or unsupported
- Potential involvement of healthcare systems and insurers, translating and communicating the impact of non-compliance into cost-benefit ratios

<i>ABOUT BREAST CANCER RECURRENCE</i>

Q. What medications can women take to reduce the risk of recurrence?

A. The medications or treatment regimen a woman will be prescribed after breast cancer depends on various factors: the stage of cancer, the type of breast cancer and grade, menopausal status, hormone receptor status and even genetics. For some women, particularly postmenopausal women, a five-year regimen of hormonal therapy may be recommended to help reduce the risk of recurrence. Patients should talk to their healthcare team about their options and participate in making the best treatment decision to reduce the risk of a breast cancer recurrence.

Q. Does improving compliance reduce a breast cancer patient’s risk of recurrence?

A. Several factors influence a woman’s particular risk for breast cancer recurrence, including: the stage of cancer at diagnosis, hormone receptor status, menopausal status

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and even genetics. In a meta-analysis of breast cancer studies, the chance of breast cancer recurrence without adjuvant treatment was highest (peaking at nearly 10 percent) within the first three years after an initial diagnosis of early breast cancer. If a breast cancer patient is a candidate for post-treatment oral hormonal therapy, studies have shown she may reduce her chance of recurrence 12 percent by staying on drug one year, 29 percent by staying on drug for two years, and 47 percent by staying on drug up to five years.⁴

Q. After five years, aren't you "cured?"

A. A woman's risk of recurrence never goes away. Patients should talk with their physicians about their treatment and risk of recurrence.

<i>ABOUT HORMONAL THERAPY</i>

Q. What is hormonal therapy?

A. Hormonal therapies interfere with the ability of a breast cancer cell to use hormones as a vehicle to grow. This interference occurs in two ways:

- Blocking the ability of estrogen to bind with a breast cancer cell through estrogen receptors on the cell's surface (this is how the hormonal therapy drug tamoxifen works.)
- Interfering with the ability of enzymes to contribute to the development of estrogen. This is how the class of drugs called aromatase inhibitors work. Because hormonal therapies travel through the bloodstream, they are able to affect cancer cells that are located anywhere in the body.

Q. When are hormonal therapies prescribed for breast cancer?

A. Breast cancer is usually diagnosed after a biopsy, where a section or the entire tumor is removed for evaluation. When it is determined that a woman has breast cancer, a pathologist will carefully analyze the tissue removed during surgery for characteristics that indicate the aggressiveness of a tumor. This analysis also determines the level of dependence that a tumor has on the hormones estrogen and progesterone. This reading, which measures the presence of hormone receptors on a cell's surface, can guide a physician in prescribing hormonal treatments for breast cancer. Tumors that rely on these hormones to grow are identified as "hormone-receptor positive." It is these types of breast cancers that studies have shown respond to therapies that decrease the production of hormones in the body or block the body's natural hormones from reaching breast cancer cells. Such hormonal treatment has been shown to help reduce the risk of breast cancer recurrence in women whose breast cancer is hormone receptor positive.

Q. If a patient has completed chemotherapy/radiation, why would she need hormonal therapy?

A. For postmenopausal women whose breast cancer is known to be hormone receptor-positive, studies have shown that additional or adjuvant treatment with hormonal therapy can reduce the risk of recurrence significantly, particularly if the women stay on drug for the recommended five-year course of treatment.

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Q. Why do breast cancer patients have to take a hormonal treatment for five years?

A. Studies have shown that for the appropriate patients, additional or adjuvant treatment with a hormonal therapy can reduce the risk of recurrence significantly, particularly if the women stay on drug for the standard, recommended five-year course of treatment.

According to a meta-analysis of randomized trials that evaluated the impact of adjuvant tamoxifen therapy for 1 year, 2 years, and approximately 5 years, the proportional recurrence reductions produced over a 10-year period were 21 percent, 29 percent and 47 percent, respectively.⁴ For longer than 5 years, it is believed that the risk of side effects may outweigh its benefit.¹²

¹ Wall Street Journal Online/Harris Interactive Health-Care Poll. Prescription Drug Compliance A Significant Challenge for Many Patients, According to New National Survey. News Release, March 29, 2005. Available at: <http://www.harrisinteractive.com/news/allnewsbydate.asp?NewsID+904>. Accessed December 8, 2005

² Partridge AH, Wang PS, Winer EP, Avorn J. Nonadherence to adjuvant tamoxifen therapy in women with primary breast cancer. *J Clin Oncol* 2003;21:602-606.

³ Fisher B, Costantino JP, Wickerham DL, et al. Tamoxifen for prevention of breast cancer: Report of the National Surgical Adjuvant Breast and Bowel Project P-1 Study. *J Natl Cancer Inst* 1998;90:1371-1388.

⁴ Early Breast Cancer Trialists' Collaborative Group. Tamoxifen for early breast cancer: An overview of the randomized trials. *Lancet*. 1998;351:1451-1467.

⁵ Osterberg L, Blaschke T. Adherence to medication. *N Engl J Med*. 2005;353:487-497.

⁶ Davidson B et al. Poster presented at: 28th Annual San Antonio Breast Cancer Symposium; December 8-11, 2005; San Antonio, Tex. Poster: P1118.

⁷ Nichols-English, G, Poirier S. Optimizing Adherence to Pharmaceutical Care Plans. *J Am Pharm Assoc*. 2000; 40:475-485.

⁸ ISPOR Medication Compliance And Persistence Special Interest Group. Standardizing Definition of terms. Available at: http://www.ispor.org/sigs/MCP_accomplishments.asp#definition

⁹ National Cancer Institute. Lifetime Probability of Breast Cancer in American Women. *SEER Cancer Statistics Review* 1973-1999.

¹⁰ American Cancer Society. Cancer facts & figures 2006. Available at: http://www.cancer.org/docroot/STT/content/STT_1x_Cancer_Facts_Figures_2006.asp. Accessed August 14, 2006.

¹¹ Partridge AH, Avorn J, Wang PS, Winer EP. Adherence to therapy with oral antineoplastic agents. *J Natl Cancer Inst*. 2002;94:652-661.

¹² Scottish Adjuvant Tamoxifen Trial: A Randomized Study Updated to 15 Years. *J Natl Cancer Inst*. 2001; 93:456-462.

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